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Impact and Effectiveness of State-level Tuberculosis interventions in California, Florida, New York and Texas: A model-based analysis.

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Abstract

The incidence of tuberculosis (TB) disease in the United States has stabilized, and additional interventions are needed to make progress toward TB elimination. But the impact of such interventions depends on local demography and heterogeneity in populations at risk. Using state-level individual-based TB transmission models, calibrated to California, Florida, New York, and Texas, we modeled two TB interventions: (i) Increased targeted testing and treatment (TTT) of high-risk populations, including people who are non-US-born, diabetic, HIV-positive, homeless, or incarcerated; and (ii) Enhanced TB contact investigation (ECI), including higher completion of preventive therapy. For each intervention, we projected reductions in active TB incidence over 10 years (2016–2026) and numbers needed to screen and treat to avert one case. TTT delivered to half of the non-US-born adult population could lower TB incidence by 19.8%–26.7% over ten years. TTT delivered to smaller populations with higher TB risk (e.g., HIV-positive, homeless) and ECI were generally more efficient, but had less overall impact on incidence. TTT targeted to smaller, highest-risk populations, and ECI can be highly efficient; however, major reductions in incidence will only be achieved by also targeting larger, moderate-risk populations. Ultimately, to eliminate TB in the US, a combination of these approaches is necessary.

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Keywords

Tuberculosis; Tuberculosis prevention in the US; Targeting TB preventative therapy; Mathematical modeling of TB

Introduction

Tuberculosis (TB) remains an important public health concern in the United States (US) with 9,272 cases in 2016 (1). Though this represents the lowest incidence rate since reporting began in 1953, the rate of decline in TB incidence is slowing (2). Model-based projections suggest that, without additional intervention, declines in TB incidence may slow even further (3,4,5).

Multiple analyses suggest that recent transmission of TB infection has declined sharply over the past two decades (6,7), such that over 70% of incident active TB now reflects reactivation of infection acquired in the distant past (8,9,10). Thus, existing TB control efforts, which have successfully reduced TB incidence – particularly TB incidence due to recent transmission (11) – may not produce ongoing similar reductions in the future. Hence, it is important to consider the potential impact of additional interventions, such as increasing targeted testing and treatment (TTT) of latent TB infection (LTBI) among high-risk populations.

There is substantial heterogeneity in TB epidemiology across the country, reflecting differences in demographics (e.g., population size and origin of non-US-born individuals (4)), prevalence of TB risk factors (e.g., HIV, diabetes, and immigration (12)), rates of reactivation, (13) and/or ongoing transmission (10). Moreover, there are differences in funding and implementation of TB prevention and control efforts. Such heterogeneities may cause the effectiveness of specific TB prevention strategies to differ between states, even when the implementation of each intervention is similar.

We therefore utilized a state-specific transmission model of TB in four states (California, Florida, New York, and Texas) to estimate the population-level impact of two TB inventions — (i) increased TTT in high-risk populations and (ii) enhanced contact investigation (ECI). These four states not only contribute over half of all incident TB cases in the United States (1), but they are diverse in their demographic makeup and prevalence of TB risk factors.

Methods

Overview

Our primary objective was to quantify the projected impact (10-year reduction in TB incidence) and efficiency (number needed to screen and treat to avert one TB case) of augmented TTT and ECI, and to illustrate the extent to which these measures vary across the four largest US states. We used a previously described individual-based modeling framework, (4) structured to capture the demographic and epidemiological processes underpinning the diverse TB epidemics in these states. We expanded this model to incorporate and calibrate to historical data on diabetes, HIV, homelessness, and

incarceration. Using this framework, we modeled the potential impact of accelerated TTT and ECI in each state, which were identified as priorities in discussions with TB controllers from all four states. For both interventions, we estimated the number of individuals who would potentially be tested and treated under ideal scale-up conditions, the reduction in annual TB incidence (per 100,000 population) and TB cases over 10 years, the number needed to screen/test (NNS) and the number needed to treat (NNT) to avert one case of TB.

Baseline model

Full details of our model of population demography and TB natural history have been described elsewhere (4). Briefly, our model classifies individuals as being in one of four TB states: (i) uninfected; (ii) LTBI; (iii) active TB, or (iv) successfully treated. Rates of infection are proportional to the fraction of individuals with active TB, under a homogeneous mixing assumption. We incorporate secular trends in TB transmission rates and age- and time-dependent reactivation rates, following previous models (14). Transmission rates and reactivation rates are calibrated to state-specific data including TB incidence, accounting for differences by age and temporal trends. The model allows for reinfection (with partial immunity following initial infection), diagnosis, and successful treatment (modeled as an instantaneous transition). Birth and death rates were calibrated to reflect each state's age distribution.

Incorporation of high-risk populations

We modeled five TB risk factors: (i) non-US region of birth; (ii) diabetes; (iii) HIV; (iv) homelessness; and (v) incarceration. We estimated the size of the population with each risk factor (Table 1) and the proportion of TB cases that occurred in each high-risk population (Fig. 1).

Rates of immigration into each state were calibrated to the size of the non-US-born population (14) across eight regions: (i) Mexico; (ii) Latin America (excluding Mexico); (iii) China; (iv) India; (v) Asia (excluding China and India); (vi) Africa; (vii) Europe; and (viii) others. (See (4) for further details). We assumed that LTBI prevalence among non- US-born individuals at arrival reflected the TB prevalence in the region of origin (i.e., that individuals experienced a constant hazard of TB infection from birth until US arrival at a rate consistent with prevalence in the region of origin). After arrival, we assumed that there were no additional differences between non-US-born and US-born individuals in terms of mixing or natural history of TB progression. Hence, we assumed that any potential differential in risk of TB among the non-US-born reflected a higher probability of LTBI on arrival, rather than an increased probability of reactivation among non-US-born individuals relative to US-born individuals with LTBI.

For the other four risk factors, we calibrated state-specific probabilities of exposure/development to the estimated prevalence of each risk factor in each state. (See Web Appendix 1, Web Table 1, and Web Figures 1–4 for details). We then made *a priori* assumptions about the mechanism of each risk factor's effect: diabetes and HIV were assumed to increase an individual's reactivation rate, whereas homelessness and incarceration were assumed to increase the rate of TB acquisition through transmission. We

calibrated the magnitude of this additional risk to risk-factor-specific TB incidence data in each state. (See Table 1 and Fig. 1 for data and model fits, and Web Table 1 for estimated magnitude of increase in state-specific risk factors).

Modeling TB interventions

We modeled two interventions, namely increased targeted testing and treatment of TB (TTT) in high-risk populations and enhanced TB contact investigation (ECI). We estimated the impact of interventions as additional changes from projected TB declines under baseline assumptions. We assumed that existing testing and treatment of LTBI resulted in 3% of individuals with untreated LTBI starting treatment annually (15), with 44% successfully completing treatment. We modeled contact investigation as evaluation of individuals from the underlying population, selected at random, but with weights reflecting the reported relative odds of active TB or LTBI among contacts compared against the general population (16). Except for this increased probability of TB/LTBI, contacts were not assumed to differ from the general population with respect to other risk factors. We assumed that TB contact investigation identified 16.9 contacts per case, with 50% of these contacts triggering contact investigations, of whom 82% were evaluated, and that 44% of individuals referred for LTBI treatment completed treatment (16). We did not consider enhancement of outbreak investigations or identification of other contacts not elicited during contact investigation. Each intervention was modeled over 10 years, and outcomes were projected over the same duration. The impact of each intervention was estimated by comparing model simulations with the intervention against corresponding simulations without the intervention.

i. *(i) Increased Targeted Testing and Treatment of TB in high-risk populations*. We modeled TTT as a one-time intervention including testing and treatment (of random selection of those with active TB and previously untreated LTBI) in five populations at high risk for TB. We assumed 85% sensitivity of testing, 66% completion of LTBI therapy, and 93% efficacy of treatment for LTBI among those who complete therapy (16,17,18).

ii. *(ii) Enhanced TB Contact Investigation*. We modeled enhanced TB contact investigation as an improvement over current estimates in the percentage of contacts evaluated (from 82% to 100%) and the percentage of contacts successfully completing LTBI treatment (from 44% to 84%). We used recent national data to estimate the number of contacts elicited and examined per index case and the odds of disease or infection among contacts (16) (Table 2).

Sensitivity Analyses

To evaluate the sensitivity of our results to variation in individual input parameters, we compared the primary outcome (percentage reduction in TB incidence) in model simulations with the parameter values in the highest decile against simulations with parameter values in the lowest decile. We performed this analysis for each intervention (including each set of population risk parameters) in each state. See Web Appendix 2, and Web Figure 5 for sensitivity of ECI; and Web Appendix 3, and Web Figures 6–9 for sensitivity of TTT). We also evaluated alternative intervention scenarios, such as treating LTBI with 3 months of isoniazid and rifapentine (see Web Appendix 4 and Web Tables 2 and 3), and doubling the

number of contacts evaluated in contact investigation (see Web Appendix 5 and Web Table 4).

Results

Targeted Testing and Treatment

The non-US-born population represented the largest target group for LTBI evaluation and treatment. We estimated that screening 50% of randomly selected non-US-born adults in each state would require, per 100,000 population, testing of 7,882 (95% range, 7,876 – 7,889) individuals in Texas; 9,698 (95% range, 9,691 – 9,707) in Florida; 10,953 (95% range, 10,944 – 10,961) in New York; and 13,379 (95% range, 13,372 –13,387) in California (Table 3). This would result in testing of approximately 2.16 million individuals in Texas, 1.96 million individuals in Florida, 2.16 million individuals in New York, and 5.22 million individuals in California (See Web Appendix 6 and 7, and Web Tables 5 and 6 for other sub-populations). Testing these people was projected to result in, per 100,000 population, 1.1 (95% range, 0.9 – 1.2) TB diagnoses (identified active TB cases among those tested) and 959 (95% range, 955 – 962) LTBI treatment completions in Texas; 1.0 (95% range, 0.8 – 1.5) TB diagnoses and 1,337 (95% range, 1,332 – 1,342) LTBI treatment completions in Florida; 1.3 (95% range, 1.2 – 1.5) TB diagnoses and 1,523 (95% range, 1,518 – 1,528) LTBI treatment completions in New York; and 3.1 (95% range, 3.0 –3.4) TB diagnoses and 2,546 (95% range, 2,542 – 2,550) LTBI treatment completions in California. Differences between states largely reflect the differences in the size of the non-US-born population (Table 1) and the relative risk of TB among those individuals (Fig 1). As shown in Table 3, targeted testing among diabetics would involve testing 58% (in California) to 100% (in Texas) as many individuals as testing the non-US-born but would generate only about one-third as many people treated (for active TB or LTBI) in each state. By comparison, screening high-risk populations consisting of HIV-positive, homeless, or incarcerated individuals was estimated to result in substantially fewer individuals tested (< 1,000 per 100,000). This resulted in fewer cases of active TB diagnosed (< 0.5 per 100,000) and fewer LTBI treatment completions (< 200 per 100,000), reflecting the lower prevalence (<1.2%) of these other risk factors (Table 1).

TTT of non-US-born populations was projected to have substantial impact in all states (Table 4), achieving the following reductions in TB incidence (in addition to expected declines in the absence of additional intervention) over a 10-year period: 19.8% (95% range, 16.9–22.9) in New York, 21.1% (95% range, 18.6–23.8) in Texas, 22.4% (95% range, 19.0–26.1) in Florida, and 26.7% (95% range, 25.2–28.2) in California. Corresponding reductions in incidence from TTT among diabetics were: 6.4% (95% range, 3.2–9.8), 7.3% (95% range, 4.6–10.5), 8.5% (95% range, 4.4–12.9), and 10.4% (95% range, 8.6–12.2). In comparison, the absolute impact of screening other high-risk populations was relatively small (no more than 6% reduction for any single risk group, in any state, except for a 10.3% reduction from TTT of HIV-positive people in Florida). This reflects the smaller size of these highest-risk populations (Table 1), which therefore account for a relatively small proportion of overall TB incidence (Fig 1).

Conversely, TTT in the non-US-born and diabetic populations was projected to be less efficient compared to screening highest-risk groups (Fig 2). For example, the estimated NNS to avert one TB case among HIV-positive individuals was 100–500, with a corresponding NNT of 10–50, whereas corresponding estimates for people with diabetes were approximately ten-fold higher (1,000–5,000 and 100–300, respectively).

There was also substantial heterogeneity in the efficiency of TTT between states, with lower NNS/NNT indicating greater effectiveness. For example, the NNS among diabetic populations was projected to be more than twice as high in Florida relative to California (turquoise bars in Fig 2, top panel), and the NNT among non-US-born populations was more than twice as high in New York relative to Texas (purple bars in Fig 2, bottom panel).

Enhanced contact investigation

We estimated the odds ratio of active TB and LTBI among contacts of active TB cases, relative to the general population, to be 1239 and 3.8, respectively. The projected yields of ECI differed substantially across the four states: we estimated 0.15 (95% range, −0.04 – 0.36) additional TB diagnoses and 15 (95% range, 14 – 16) additional LTBI treatment completions in Florida versus 0.36 (95% range, 0.11 – 0.60) additional TB diagnoses and 51 (95% range, 49 – 52) additional LTBI treatment completions in California, per 100,000 population (Table 5). The projected impact of ECI on TB incidence was modest and subject to considerable uncertainty. The corresponding projected 10-year reductions in incidence ranged from 0.01% in New York to 0.67% in California, but the 95% uncertainty range included 0% in all four states. Nevertheless, point estimates suggested that ECI is likely to be an efficient intervention, with NNT less than 200 in all states (Figure 2).

Discussion

In these models of TB transmission in the four US states that contribute to more than half of new TB cases, we incorporated state-level data on demography, TB incidence, and size of high-risk populations to quantify the projected impact and efficiency of targeted testing and treatment and expanded contact investigation. Our results suggest that accelerating TTT and expanding contact investigation can generate meaningful reductions in TB incidence, but the impact and efficiency of these interventions is likely to differ across states. Those interventions that achieve the largest population-level impact (e.g., TTT of non-US-born and diabetic populations) differ from those that are most efficient (e.g., ECI and TTT of HIV-positive, homeless, and incarcerated populations). Ultimately, if TB is to be eliminated in the US, a combination of these approaches is likely to be necessary.

Contact investigation has served a critical role in achieving reductions in TB incidence to date. However, our work suggests that further expansion of contact investigation is unlikely to have major additional population-level impact in terms of further reducing TB incidence – largely because existing efforts are already reasonably comprehensive. ECI remains critical, however, in maintaining low rates of TB transmission in high-risk populations and averting future outbreaks of disease (19).

Progress in further reducing TB incidence is likely to hinge on success in implementing TTT in high-risk populations. Our study revealed important state-level heterogeneity in projected impact (and efficiency) of TTT. For example, the maximum impact of TTT (in all high-risk populations) was about 20% lower in New York compared to California. This was more pronounced in smaller risk groups: for example, TTT of HIV-positive individuals could avert four times as many TB cases in Florida compared to California. Heterogeneity in projected impact was accompanied by heterogeneity in projected efficiency between states – reflecting between-state differences in TB incidence, LTBI prevalence, prevalence of risk factors, and strength of risk factors (in terms of their association with TB). In prioritizing interventions at the state level, it is important to take such heterogeneities into account. Prioritization of TB elimination activities such as TTT and ECI involves diverse stakeholders, including TB controllers at the state level, and primary care providers and specialized agencies (e.g., federally qualified health centers, correctional facilities). Each of these stakeholders must balance multiple considerations – such as budgetary constraints and political will – in deciding how to allocate resources. Collaboration between these stakeholders is critical if TB elimination is to be achieved; recognition of heterogeneities in transmission at the state level may help to facilitate such collaboration.

This study has important limitations. As there were no primary data on state-specific LTBI prevalence, we estimated this prevalence indirectly by calibrating the model to other available data (e.g., state-level demographics and TB incidence). Our estimates are comparable with other recent estimates of LTBI prevalence in these four states (20). (See Web Appendix 8, Web Figure 10, and Web Table 7). Similarly, state-specific data on historical state-level TB control efforts, including TTT and CI, were not available. We therefore assumed that state-specific levels of these activities reflected national estimates (16). State-specific contact investigation indicators for 2015 reveal that there might be significant differences in contact investigation performance: for example, 61% of identified contacts started treatment, and 73% completed treatment in California, versus 68% and 67% in Texas, 80% and 66% in Florida, and 81% and 77% in New York. However, sensitivity analysis (Web Appendix 2) shows that these variations likely have little effect on the modeled impact of ECI in these four states. We compiled data on high-risk populations from several sources; numerators (from the NTSS database) and denominators (Table 2) of our incidence estimates may be subject to different biases and uncertainties and did not include overlap between different risk groups. Finally, we were unable to analyze TTT by both birthplace and diabetes; TTT is likely to be more efficient among non-US-born persons than among US-born persons with diabetes (21).

We made several simplifying modeling assumptions, including our implicit hypothesis that historical trends in TB declines were primarily driven by reductions in TB transmission (as opposed to, e.g., declines in reactivation rates). While secular declines in reactivation rates (per person-year among people with LTBI) have been suggested over longer time frames (22), these declines are less likely to affect 10-year projections. The low levels (< 15%) of recent transmission in the United States observed using TB genotyping data corroborate this assumption (13). We modeled some age-specific differences in reactivation rates, but focused on the differences during early years of life. We also made simplifying assumptions regarding how different risk factors modulated TB risks (i.e., by reducing risk of acquisition

versus reactivation), and we assumed that US- and non-US-born populations only differed in their LTBI prevalence (i.e., not in the risk of reactivation, among those with LTBI), consistent with other estimates (8). We assumed that LTBI prevalence among non-US-born individuals at arrival reflects the TB prevalence in the country/region of origin (4). The non-US-born population is a diverse group, and LTBI prevalence among immigrants to the US can differ from their age-matched LTBI prevalence in home countries (23,24). Because our model is calibrated to TB incidence (rather than LTBI prevalence) in the US, our estimates of intervention impact are relatively robust to LTBI prevalence estimates (see Web Appendix 9, and Web Table 8). Furthermore, available data (23) show strong correlation between TB incidence among non-US-born populations in the US and TB incidence in the country of origin (particularly among recent migrants), as well as higher incidence among recent arrivals (see Web Appendix 10, and Web Figure 11), suggesting that our model assumptions, though simplistic, are reasonable to a first approximation.

In our model of enhanced contact-investigation, we did not capture potentially important differences between contacts and other individuals with (latent or active) TB, such as nativity, presence of other risk factors (e.g., homelessness), or the risk of TB progression, which may be higher owing to the possibility of recent infection. Consequently, these estimated impact of ECI are likely conservative. While the uncertainty ranges for the projected population-level impact of ECI likely still cross zero, our estimated NNT for ECI may be an overestimate. These findings may also not necessarily generalize as well to other states, especially states (e.g., those in the Southeast) that have lower proportions of non-US-born individuals and higher proportions of TB due to recent transmission. We modeled idealized interventions, assuming it was feasible to identify populations for testing and achieve large-scale implementation; thus, our results should be interpreted as the potential impact from broad scale-up of these interventions on the population level, not the actual impact likely to be observed from implementing these interventions under more realistic conditions. TTT in non-US-born and diabetic populations were modeled to be deployed in a random fashion: prioritizing higher risk subpopulations (e.g., recent arrivals to the US) may further increase this estimated impact. Finally, in our projections, we did not account for potential future demographic shifts, including changes in the sizes of the populations analyzed or potential declines in TB prevalence globally; these shifts are likely to be small on a 10-year time frame.

In summary, this state-specific TB model suggests that expanded TB interventions, particularly TTT of high-risk populations, can play an important role in reducing TB incidence over the next 10 years. However, the impact and efficiency of these interventions likely vary across risk groups and across states. Targeting smaller high-risk populations such as HIV-positive and homeless populations is likely to yield greater impact per person screened (or treated), but these populations are not large enough to effect substantial reductions in TB incidence at a population level. TTT of non-US-born and particularly diabetic populations is less efficient on a per-person-screened basis, but these populations contribute large numbers of TB cases, such that averting these future cases can result in substantial reductions in TB incidence. There are also important differences in the impact and efficiency of TB interventions between states, driven by state-level differences in prevalence of populations at risk for TB, LTBI prevalence in each population, and TB

transmission and reactivation rates. Accounting for these differences across risk groups and between states may help to improve the impact and efficiency of TB interventions that are often implemented at the state level.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ECI	enhanced contact investigation
HIV	human immunodeficiency virus
LTBI	latent tuberculosis infection
NNS	numbers needed to screen
NNT	numbers needed to treat
TB	tuberculosis
TTT	targeted testing and treatment of tuberculosis

References

1. Centers for Disease Control and Prevention (CDC). Reported Tuberculosis in the United States, 2016 Atlanta, GA: US Department of Health and Human Services, CDC; 2017.
2. Salinas JL, Mindra G, Haddad MB, Pratt R, Price SF, Langer AJ. Leveling of Tuberculosis Incidence – United States, 2013–2015. Morbidity and Mortality Weekly Report (MMWR). 2016;65:273–278. [PubMed: 27010173]
3. Hill AN, Becerra JE, Castro KG. Modelling tuberculosis trends in the USA. Epidemiol Infect. 2012;140:1862–1872. [PubMed: 22233605]
4. Shrestha S, Hill AN, Marks SM, Dowdy DW. Comparing drivers and dynamics of tuberculosis (TB) in California, Florida, New York and Texas. Am J Respir Crit Care Med. 2017;196(8):1050–1059. [PubMed: 28475845]
5. Menzies NA, Cohen T, Hill AN,Yaesoubi R, Galer K, Wolf E, Marks SM, Salomon JA. Prospects for Tuberculosis elimination in the United States: Results of a Transmission Dynamic Model. American Journal of Epidemiology. 2018;187(9):2011–2020 [PubMed: 29762657]

6. France AM, Grant J, Kammerer JS, Navin TR. A field-validated approach using surveillance and genotyping data to estimate tuberculosis attributable to recent transmission in the United States. American Journal of Epidemiology. 2015;182(9):799–807 [PubMed: 26464470]
7. Fojo AT, Stennis NL, Azman AS, Kendall EA, Shrestha S, Ahuja, SD, Dowdy DW. Current and future trends in tuberculosis indicidence in New York City: a dynamic modelling analysis. Lancet Public Health. 2017;2:e323–30. [PubMed: 29082351]
8. Mancuso JD, Diffenderfer JM, Ghassemieh BJ, Horne DJ, Kao TC. The Prevalence of Latent Tuberculosis Infection in the United States. Am J Respir Crit Care Med 2016; 194(4):501–109. [PubMed: 26866439]
9. Tsang CA, Langer AJ, Navin TR, Armstrong LR. Tuberculosis Among Foreign-born Persons Diagnosed 10 ≥ 10 years After Arrival in the United States, 2010–2015. MMWR Morb Mortal Wkly Rep 2017; 66:295–298. [PubMed: 28333913]
10. Yuen CM, Kammerer JS, Marks K, Navin TR, France AM. Recent Transmission of Tuberculosis—United States, 2011–2014. PLoS One. 2016; 11(4):e0153728 [PubMed: 27082644]
11. Mindra G, Wortham JM, Haddad MB, Powell KM. Tuberculosis Outbreaks in the United States, 2009–2015. Public Health Reports. 2017; 132(2):157–163. [PubMed: 28147211]
12. Cherng ST, Shrestha S, Reynolds S, Hill AN, Marks SM, Kelly J, Dowdy DW. Tuberculosis incidence among populations at high risk in California, Florida, New York and Texas, 2011–2015. American Journal of Public Health. 2018; 108(S4):S211–314.
13. Shea KM, Kammerer JS, Winston CA, Navin TR, Horsburgh Jr. CR. Estimated rate of reactivation of latent tuberculosis infection in the United States, overall and by population subgroup. Am J Epidemiol. 2014;179(2):216–225. [PubMed: 24142915]
14. Vynnycky E, and Fine P. The natural history of tuberculosis: The implications of age-dependent risks of disease and the role of reinfection. Epidemiol Infect.1997;119(2):183–201. [PubMed: 9363017]
15. Sterling TR, Bethel J, Goldberg S, Weinfurter P, Yun L, Horsburgh CR and Tuberculosis Epidemiologic Studies Consortium. The scope and impact of treatment of latent tuberculosis Infection in the United States and Canada. American Journal of Respiratory and Critical Care Medicine. 2006; 173(8):927– 931. [PubMed: 16424442]
16. Young KH, Ehman M, Reves R, Maddox BLP, Khan A, Chobra TL, Jereb J. Tuberculosis Contact Investigations—United States, 2003–2012. MMWR Morb Mortal Wkly Rep. 2016; 64(50–51): 1367–74.
17. Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bilven-Sizemore E, et al. Three months of rifapentine and isoniazid for latent tuberculosis infection. New England Journal of Medicine. 2011;365(23):2155–2166. [PubMed: 22150035]
18. International Union Against Tuberculosis Committee on Prophylaxis. Efficacy of various durations of isoniazid preventive therapy for tuberculosis: five years of follow-up in the IUAT trial. Bull World Health Organ 1982;60:555–64. [PubMed: 6754120]
19. Reichler MR, Khan A, Sterling TR, Zhao H, Moran J, McAuley J, et al. Risk and Timing of Tuberculosis among close contacts of persons with infectious tuberculosis. The Journal of Infectious Diseases. 2018;218(6):1000–1008. [PubMed: 29767733]
20. Haddad MB, Raz KH, Lash TL, Hill AN, Kammerer JS, Winston CA, Castro KG, Gandhi NR, Navin TR. Emerging Infectious Diseases. 2018; 24(10):1930–1933. [PubMed: 30226174]
21. Demlow SE, Oh P, Barry PM. Increased risk of tuberculosis among foreign-born persons with diabetes in California, 2010–2012. BMC public health. 2015;1:263
22. Horsburgh CR Jr, O'Donnell M, Chamblee S, Moreland JL, Johnson J, Marsh BJ et al. Revisiting Rates of Reactivation Tuberculosis: A population-based approach. Am J Respir Crit Care Med. 2010; 182:420–425 [PubMed: 20395560]
23. Menzies NA, Hill AN, Cohen T, Salomon JA. The impact of migration on tuberculosis in the United States. The International Journal of Tuberculosis and Lung Disease. 2018;22(12):1392–403 [PubMed: 30606311]
24. Nnadi CD, Anderson LF, Armstrong LR, Stagg HR, Pedrazzoli D, Pratt R, Heilig CM, Abubakar I, Moonan PK. Mind the gap: TB trends in the USA and the UK, 2000–2011. Thorax. 2016;71:356–363. [PubMed: 26907187]

25. Census Bureau US; American Community Survey, 2015 American Community Survey 5-year Estimate. Accessed on March 14, 2017 at https://factfinder.census.gov
26. United States Diabetes Surveillance System (USDSS). National Center for Chronic Disease Prevention and Health Promotion - Division of Diabetes Translation; Centers for Disease Control and Prevention. Accessed on Nov 27, 2017 at https://www.cdc.gov/diabetes/data/
27. Centers for Disease Control and Prevention. NCHHSTP AtlasPlus. Accessed on March 14, 2017 at https://gis.cdc.gov/grasp/nchhstpatlas/main.html
28. US Department of Housing and Urban Development. One-Year Estimates of Homelessness. 2013–2015.
29. Carson EA, Mulako-Wangota J. Bureau of Justice Statistics. Counts of total jurisdiction population. Generated using the Corrections Statistical Analysis Tool (CSAT)-Prisoners on 3 14, 2017 at https://www.bjs.gov
30. Miramontes R, Hill AN, Yelk Woodruff RS, Lambert AL, Navin TR, Castro KG, LoBue PA. Tuberculosis Infection in the United States: Prevalence Estimates from the National Health and Nutrition Examination Survey, 2011–2012. PLoS ONE. 2015;10(11):e0140881 [PubMed: 26536035]

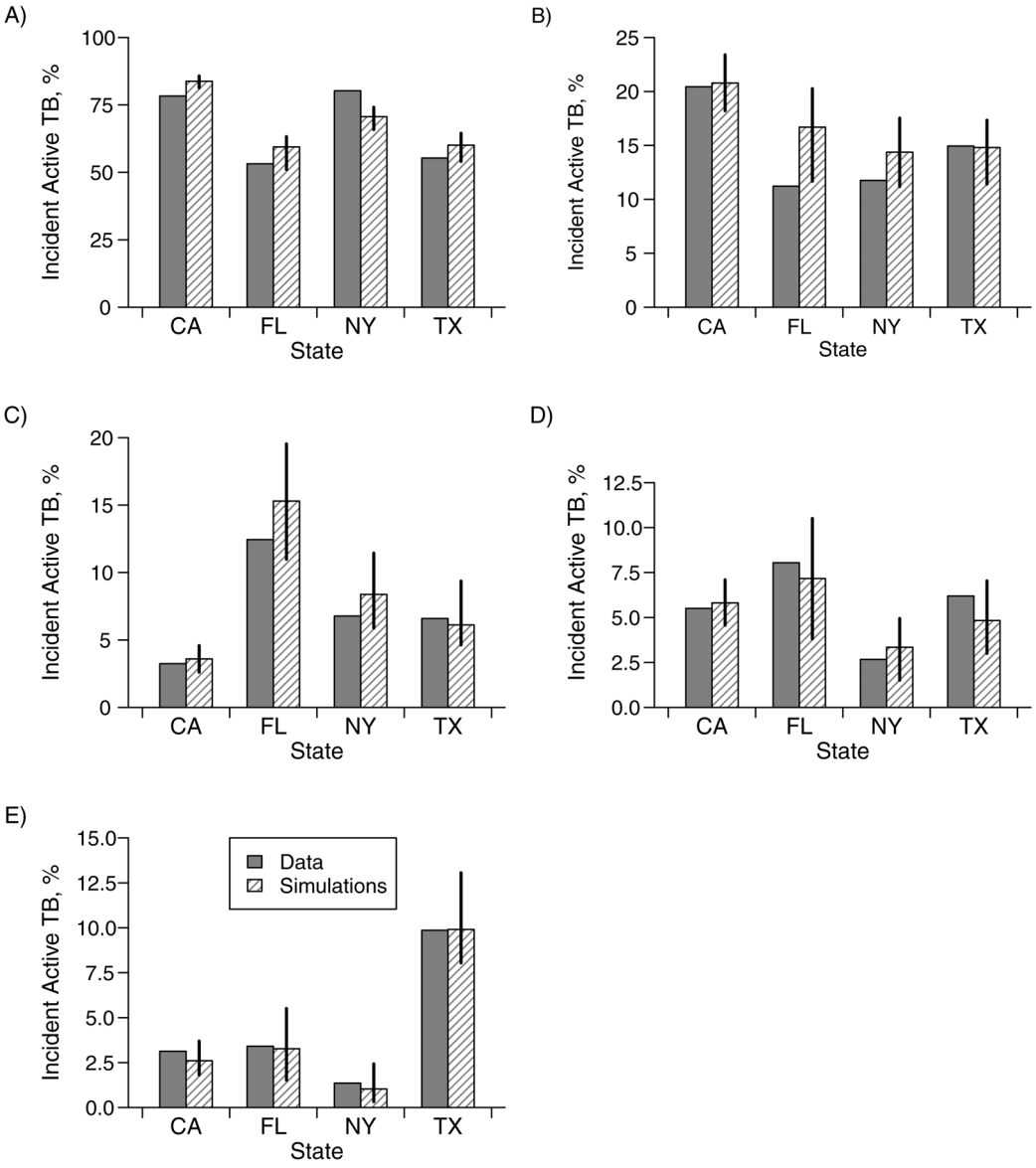

Figure 1. Percentage of incident TB cases occurring among populations with selected risk factors in California, Florida, New York, and Texas.

Shown are the percentages of reported TB cases in five risk groups, namely (A) non-US-born, (B) diabetic, (C) HIV-positive, (D) homeless and (E) incarcerated individuals, in four states: California, Florida, New York, and Texas (from left to right). Solid bars indicate reported data (averaged over 5 years from 2010 to 2014), with model simulations in hatched bars (and error bars corresponding to 95% ranges). Note the different scales of the y-axis for the non-US-born and diabetic populations, indicating their larger relative size.

Abbreviations: HIV, human immunodeficiency virus; TB, tuberculosis.

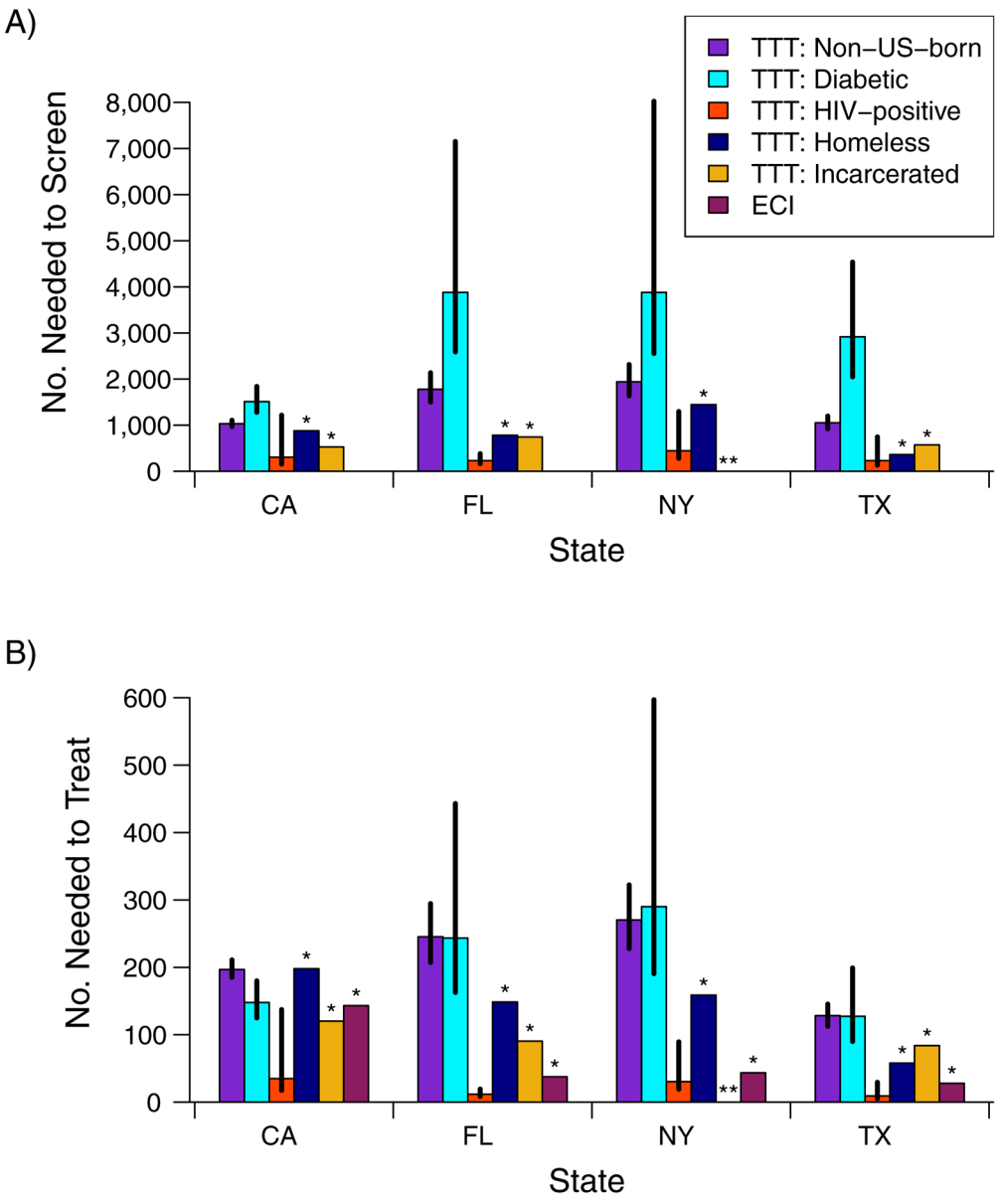

Figure 2. Comparative efficiency of TB interventions in California, Texas, New York, and Florida.

Shown in the top panel are the estimated numbers of individuals needed to screen (NNS) to avert one case of active tuberculosis (TB) for targeted testing and treatment (TTT) of latent TB infection (LTBI) among individuals who are non-US-born (purple), diabetic (turquoise), HIV-positive (red), homeless (blue), and incarcerated (yellow); and also for expanded contact investigation (ECI, maroon). Results are shown separately for each of the four largest states: California, Florida, New York, and Texas. Shown in the bottom panel are the estimated numbers of individuals needed to be treated (NNT) to avert a single case of TB. Shown are median estimates (indicated by the colored bars), along with 95% ranges (indicated by the lines). Bars with asterisks denote risk groups for which meaningful point estimates (bars with **) or 95% ranges (bars with *) could not be estimated due to small

population sizes. Note that NNS are not applicable for ECI, since it was modeled as increased evaluation rates and improved LTBI treatment completion rates among already identified contacts, with no additional screening. Abbreviations: ECI, enhanced contact investigation; HIV, human immunodeficiency virus; LTBI, latent tuberculosis infection; NNS, numbers needed to screen; NNT, numbers needed to treat; TB, tuberculosis; TTT, targeted testing and treatment of tuberculosis.

Table 1.

Estimated size of different high TB risk groups in California, Florida, New York and Texas, as a percentage of the total population, 2010–2014.

States	Non-US-born[a]	Diabetic[a]	HIV-positive[a]	Homeless[a]	Incarcerated[a]
California	27.1	9.6	0.4	0.8	0.4
Florida	19.5	10.9	0.6	0.5	0.5
New York	22.4	8.9	0.8	1.1	0.3
Texas	16.5	10.5	0.3	0.3	0.7

Abbreviation: HIV, human immunodeficiency virus.

[a]Estimates were based on the following data sources: Non-US-born (25); Diabetic (26); HIV-positive (27); Homeless (28); and Incarcerated (29).

Table 2.

Estimated Model Parameters Related to Enhanced Contact Investigation (ECI).

Level	Percentage of current TB cases that trigger contact investigations	Number of contacts elicited per case	Percentage of contacts evaluated	Estimated odds of active TB due to recent transmission, comparing contacts to the general population	Estimated odds of LTBI, comparing contacts to the general population	Percentage of contacts referred for LTBI treatment who complete therapy
Baseline	50[a]	16.9[b]	82[c]	1239[d]	3.8[e]	44[f]
Enhanced	50	16.9	100	1239	3.8	84

Abbreviations: LTBI, latent tuberculosis infection; TB, tuberculosis.

[a]Estimate based on (16);

[b]Estimate based on (16);

[c]Estimate based on (16);

[d]Estimate based on (13,16);

[e]Estimate based on (16,30);

[f]Estimate based on (16);

Table 3.

Projected yields (numbers of individuals per 100,000 population) of targeted testing and treatment (TTT) for tuberculosis in California, Texas, New York, and Florida.

Population	California		Florida		New York		Texas	
	Point Estimate	95% Range	Point Estimate	95% Range	Point Estimate	95% Range	Point Estimate	95% Range
Non-US-born[a]								
Individuals screened	13,379	13,372, 13,387	9,698	9,691, 9,707	10,953	10,944, 10,961	7,882	7,876, 7,889
Diagnoses of active TB	3.1	3.0, 3.4	1.0	0.8, 1.5	1.3	1.2, 1.5	1.1	0.9, 1.2
LTBI treatment completed	2,546	2,542, 2,550	1,337	1,332, 1,342	1,523	1,518, 1,528	959	955, 962
Diabetic[b]								
Individuals screened	7,764	7,757, 7,772	8,349	8,337, 8,360	7,567	7,557, 7,576	7,882	7,875, 7,889
Diagnoses of active TB	1.1	1.0, 1.2	0.3	0.3, 0.4	0.3	0.2, 0.4	0.4	0.3, 0.4
LTBI treatment completed	758	755, 760	523	518, 528	564	560, 569	344	342, 347
HIV-positive[c]								
Individuals screened	358	356, 360	601	598, 604	692	689, 696	332	330, 334
Diagnoses of active TB	0.20	0.17, 0.24	0.49	0.38, 0.59	0.29	0.22, 0.36	0.19	0.14, 0.24
LTBI treatment completed	41	40, 41	30	30, 31	47	46, 48	13	12, 14
Homeless[c]								
Individuals	776	773, 778	545	542, 549	965	961, 969	270	268, 272
screened Diagnoses of active TB	0.36	0.29, 0.42	0.13	0.08, 0.18	0.09	0.05, 0.13	0.14	0.10, 0.18
LTBI treatment completed	174	173, 175	103	102, 105	106	105, 108	43	42, 44
Incarcerated[c]								
Individuals screened	379	377, 382	526	523, 529	272	270, 274	645	643, 648
Diagnoses of active TB	0.17	0.13, 0.21	0.06	0.03, 0.10	0.02	0.00, 0.04	0.26	0.20, 0.33
LTBI treatment completed	86	85, 87	64	63, 65	35	34, 35	94	93, 95
All Target Populations[d]								
Individuals screened	20,571	20,561, 20,582	18,023	18,009, 18,037	18,648	18,637, 18,662	15,754	15,742, 15,765
Diagnoses of active TB	4.3	4.0, 4.5	1.6	1.4, 1.8	1.8	1.6, 2.0	1.7	1.6, 1.9
LTBI treatment completed	3,173	3,168, 3,178	1,809	1,801, 1,817	2,017	2,008, 2,025	1,283	1,279, 1,287

Abbreviations: HIV, human immunodeficiency virus; LTBI, latent tuberculosis infection; TB, tuberculosis.

[a] Assuming 50% coverage (randomly selected) among all non-US-born adults in each state.

[b] Assuming 80% coverage (randomly selected) among all individuals with diabetes in each state.

[c] Assuming coverage including the entire population of the associated risk factor in each state.

[d] Assuming coverage of all the above risk groups, at the specified level for each group.

Table 4.

Projected achievable 10-year reduction in TB incidence under increased targeted testing and treatment and enhanced contact investigation interventions.

Population	California		Florida		New York		Texas	
	% Reduction	95% Range	% Reduction	95% Range	% Reduction	95% Range	% Reduction	95% Range
Targeted Testing and Treatment								
Non-US-born	26.7	25.2, 28.2	22.4	19.0, 26.1	19.8	16.9, 22.9	21.1	18.6, 23.8
Diabetic	10.4	8.6, 12.2	8.5	4.4, 12.9	6.4	3.2, 9.8	7.3	4.6, 10.5
HIV-positive	2.1	0.2, 4.1	10.3	6.2, 14.3	5.1	1.6, 8.5	3.6	0.8, 6.7
Homeless	1.4	−0.7, 3.4	1.6	−2.7, 5.7	0.7	−2.6, 4.2	1.0	−2.2, 4.0
Incarcerated	0.7	−1.5, 2.6	0.8	−3.3, 5.0	−0.5	−4.0, 3.0	2.7	−0.3, 5.8
All risk groups combined[a]	35.8	34.2, 37.2	35.8	32.9, 38.8	28.5	25.7, 31.3	31.2	29.0, 33.6
Enhanced Contact Investigation								
	0.67	−1.31, 2.49	0.39	−3.75, 4.63	0.01	−3.12, 3.32	0.12	−3.20, 3.15

Abbreviations: HIV, human immunodeficiency virus.

[a]Does not equal the sum of the five individual risk groups largely because individuals with more than one risk factor only receive the intervention once.

Table 5.

Projected yields (numbers of individuals per 100,000 population) of expanded contact investigation in four key states per year.

Population	California		Florida		New York		Texas	
	Point Estimate	95% Range	Point Estimate	95% Range	Point Estimate	95% Range	Point Estimate	95% Range
Non-US-born[a]								
Additional diagnoses of active TB	0.36	0.11, 0.60	0.15	−0.04, 0.36	0.13	−0.05, 0.31	0.23	0.02, 0.44
Additional number of LTBI treatment completions	51	49, 52	15	14, 16	22	20, 23	14	13, 15

Abbreviations: LTBI, latent tuberculosis infection; TB, tuberculosis.